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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,107	11/20/2003	Michael P. Girouard	P03155US (98554.1P3)	8886

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EXAMINER	
CHUI, MEI PING	
ART UNIT	PAPER NUMBER
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/718,107	GIROUARD, MICHAEL P.	
	Examiner	Art Unit	
	Helen Mei-Ping Chui	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48,55,85,86,91,116,117,119 and 124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48,55,85,86,91,116,117,119 and 124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/28/2004 & 06/23/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Action

The Examiner acknowledges receipt of application number 10/718107 filed on 11/20/2003 and amended Claims on 04/23/2004. Claims 48, 55, 85-86, 91, 116-117, 119 and 124 were amended. Claims 1-47, 49-54, 56-84, 87-90, 92-115, 118, 120-123, 125-137 were cancelled. Accordingly, claims 48, 55, 85-86, 91, 116-117, 119 and 124 are presented for examination on the merits for patentability.

DOUBLE PATENTING

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 48 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 6,821,961. This is a statutory double patenting rejection. To obviate this rejection, canceling Claim 48 is recommended.

DOUBLE PATENTING

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 48, 55, 85, 91, 116, 119 and 124 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1, 4-6 and 9 of U.S. Patent No. 6,821,961. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of claims of U.S. Patent No. 6,821,961 the instantly claimed subject matter where both claims are drawn to a method of lowering body weight in a mammal comprising administering to said mammal an effective amount of a substantially pure fatty acid monoester of an estrogen and a fatty acid. Although instant claims are differ from US Patent No.

6,821,961 because the estrogen derivative in the instant invention incorporated a hydroxyl group at the C2 position of an estrone. Nevertheless, the precursor of an estrogen derivative is the same molecule, perhydrocyclopentanophenanthrene, taught in Claims 5 and 6 of the U.S. Patent No. 6,821,961. In addition, Claims 4 and 9 of the U.S. Patent No. 6,821,961 which require the steroidal estrogen with a hydroxyl group at C-3 position of the steroid ring system attached to the monounsaturated fatty acid via an ester linkage, encompasses the instant Claims 55, 91 and 124. Because they describe estrogen is steroidal and has a steroid ring system with a hydroxyl group at C-3 position attached to the fatty acid monoester. Therefore, one of ordinary skill in the art, at the time the claimed invention was made, would have readily recognized that the claims found in both U.S. Patent No. 6,821,961 and instant application are obvious variant and are not patentability distinct to each other.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 48, 55, 85-86, 91, 116-117, 119 and 124 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alemany et al. (U. S. Patent No. 5,798,348) in view of Zhu et al. (Carcinogenesis, 1998, 19, page 1-27).

Alemany et al. report on the efficacy of an estrogen fatty acid monoester known as estrone monooleate for the treatment of obesity and/or overweight in mammals (U.S. Patent No. 5,798,348: column 1, line 6-8; column 2, line 16-18; column 3, line 34-36).

With respect to Claims 48, 55, 85-86, 91, 116-117, 119 and 124 of the instant application, the Alemany et al. '348 Patent does not teach the present of 2-hydroxyl group in estrone for treating overweight.

Zhu et al. teach that the 2-hydroxylation of estrone to 2-hydroxyestrone is a major metabolic pathway that occurs in the liver by cytochrome P450 hydroxylase. Once formed, 2-hydroxyestrone is rapidly undergoes conjugative metabolism followed by urinary excretion.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combined the oleoyl-estrone which has a body weight lowering effect, as suggested by Alemany et al. and 2-hydroxylation of an estrone, as suggested by Zhu et al. to produce the instant invention.

One of ordinary skill in the art would have been motivated to modify this because metabolite of estrone is in fact an active species which is responsible for pharmacology

action. Since Alemany et al. suggest estrone conjugated with a fatty acid moiety at C3 position is useful as an anti-obesity agent and Zhu et al. suggest 2-hydroxyestrone is a major metabolite of estrone, from the teachings of the combined references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Claim Rejection - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 48, 55, 85, 91,116, 119 are rejected under 35 U.S.C. 102(b) as being anticipated by Alemany (U.S. Patent NO. 5,798,348 on August 25, 1998).

Alemany et al. report on the efficacy of [3(Z)]-3-[(1-oxo-9-octadecenyl)oxy]estra-1,3,5(10)-trien-17-one, an estrogen fatty acid monoester known as estrone monooleate, for therapeutic and/or cosmetic treatment of obesity and/or overweight in mammals (U.S. Patent No. 5,798,348: column 1, line 6-8; column 2, line 16-18; column 3, line 34-36).

Alemany et al. teach that the estrogen in their invention consisted of natural, semi synthetic and synthetic, both steroidal and nonsteroidal; for examples estrone, diethylstilbestrol, estriol, estradiol and ethinyl estradiol (U.S. Patent No. 5,798,348: column 1, line 57-59; column 2, line 1-6; column 7, claims 1, 6 and 7). Alemany et al. also teach that the fatty acid in their invention consisted of oleic, linoleic, linolenic, stearic, palmitic, palmitoleic and arachidonic acids (U.S. Patent No. 5,798,348: column 1, line 60-63; column 2, line 7-9; column 7, claims 1, 6 and 7), where the acyl group of the fatty acid is attached to the hydroxyl group at C-3 position of the estrogen to form the fatty acid monoester by an ester linkage (U.S. Patent No. 5,798,348: column 2, line 10-12; column 7, claims 1, 6-7 and 20). All the critical elements require by instant claims are taught by cited reference; therefore, instant claims 48, 55, 85, 91,116 and 119 are anticipated.

Claim Rejection - 35 U.S.C. § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of enablement of the Invention

Claims 48, 55, 85-86, 91, 116-117, 119 and 124 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using estrone eicosenoate for the method of lowering body weight in a mammal (See Summary, page 3) does not reasonably provide enablement for using substantially pure 2-hydroxyestrone eicosenoate in the aforementioned method. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

An analysis of whether the scope of a particular claim(s) is actually supported by the disclosure in a patent application requires a determination of whether the disclosure, at the time of filing, contained sufficient information regarding the subject matter of the claim at issue so as to enable one skilled in the pertained art to use the claimed invention without undue experimentation. *In re Wands*, 8 USPQ 2d 140 (Fed. Cir. 1988). Therefore, the test of enablement is not whether experimentation is necessary, but rather, if experimentation is in fact necessary, whether it is reasonably considered to be undue. *In re Angstadt*, 190 USPQ 214, 219 (CCPA 1976). Determining the issue of enablement with respect to a claim is a question of law based on underlying factual findings. *In re Vaeck*, 20 USPQ 2d, 1444 (Fed. Cir. 1991). More particularly, there are many factors to be considered in determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, and whether any necessary experimentation is reasonably considered to be "undue". See *In re Wands* at page 1404. MPEP §

2164.01(a). The court in *In re Wands* set forth the following factors to be considered, which included, without limitation, the: 1. scope or breadth of the claims; 2. nature of the invention; 3. relative level of skill possessed by one of ordinary skill in the art; 4. state of, or the amount of knowledge in, the prior art; 5. level or degree of predictability, or a lack thereof, in the art; 6. amount of guidance or direction provided by the inventor; 7. presence or absence of working examples; and 8. quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure.

The specification fails to provide scientific data with respect to the composition of 2-hydroxyestrone eicosenoate used in the instant claims, as well as the corresponding method of making this new fatty acid monoester of 2-hydroxyestrone. Specifically, the chemical structures between an estrone eicosenoate (See U.S. Patent No. 6,821,961) and a 2-hydroxyestrone eicosenoate are different by additional hydroxyl functionality present at C-2 position. It is known to one skilled in the relevant art that the chemical reactivity of the two hydroxyl groups, 2-hydroxyl and 3-hydroxyl in 2-hydroxyestrone, is relatively similar. In fact, Nakagawa suggested that the C-2 hydroxyl group of 2-hydroxyestrogen is slightly more basic than the C-3 hydroxyl group and hence, the in vitro *O*-methylation gives the 2-methyl ether in three times larges amount than the 3-methyl ether (See Nakagawa et al. J. Pharm. Dyn. 1979, 2, 365-373). Thus, a reaction simply combining the activated fatty acid acyl chloride and 2-hydroxyestrone, as described in the specification, will not render a substantially pure 2-hydroxyestrone monoester, but a mixtures of 2-*O*, 3-*O* and 2,3-*O*-conjugated products. Fishman et al.

has been demonstrated that, in vivo, the selectivity of these two indistinguishable phenolic hydroxyl groups appear to be specific due to the enzymatic participation (J.A.C.S. 1967, 89, 7147-7148; J.O.C. 1968, 33, 662-664; Biochemistry, 1969, 8, 1669-1672); however, in vitro, this is considerably more challenging for one skilled in the relevant art to achieve such regioselectivity without any protecting strategy for the preparation of 2-hydroxyestrone eicosenoate in the claimed invention. In fact, applicant explicitly pointed out that the 2-hydroxyestrone eicosenoate is tested to be unstable and found not suitable to be use in the instant invention presumably due to the presence of undesired products and impurity in the product (See Specification, Example 12, Page 49, line 21-23). In addition, Seeger et al. also observed that 2-hydroxyestrone is rapidly oxidized in air in their experiments; thus special handling and procedures are required when utilizing 2-hydroxyestrone in their experiments (Life Science, 1997, 61, 865-868). Therefore, a substantially pure fatty acid monoester claimed in the instant invention is not enabled without further evidences to support its enabling.

It is readily apparent from the aforementioned disclosure, a great deal of uncertainty with respect to the composition used in the claimed invention; in conjunction with a corresponding lack of scientific data and direction regarding the method of lowering body weight in a mammal; as a result, one of ordinary skill in the art would therefore be required to conduct an undue amount of experimentation to reasonably and accurately extrapolate whether the said composition and corresponding method of the instant claims do in fact effectively lowering body weight in a mammal. Therefore, Applicant is required to provide in the specification additional guidance and direction

with respect to the preparation, as well as the effectiveness of the claimed subject matter in claims 48, 55, 85-86, 91, 116-117, 119 and 124 in order for the application to be enabled with respect to the full scope of the claimed invention.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48, 55, 85, 86, 91, 116, 117, 119 and 124 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially pure" in claims is a relative term which renders the claim indefinite. The term "substantially pure" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Conclusion

No claims are allowed.

Contact Information

Any inquiry concerning this communication from the Examiner should direct to Helen Mei-Ping Chui whose telephone number is 571-272-9078. The examiner can normally be reached on Monday-Friday (7:30 am – 5:00 pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where the application or proceeding is assigned is 571-273-9078.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either PRIVATE PAIR or PUBLIC PAIR. Status information for unpublished applications is available through PRIVATE PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the PRIVATE PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

HC

VICKIE KIM
PRIMARY EXAMINER